REMARKS / ARGUMENTS

This amendment is submitted as a submission with an RCE in response to the final office action of November 26, 2008. Applicant has amended Claims 11 and 17 and canceled Claim 13, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Support for the amendment to Claims 11 and 17 may be found throughout the specification, for example, in Claim 13 as originally filed. Favorable consideration of all pending claims is respectfully requested.

In the final office action of November 26, 2008, Claims 11-14 and 16-19 remain rejected under 35 U.S.C. §102(b) as allegedly anticipated by Posanski (GB 2 228 198 A).

Posanski has been cited for allegedly teaching pharmaceutical compositions containing cyclosporine, a carrier composition that contains oils, and a tenside having an HLB of 10 and Cremophor. The Examiner has asserted that on page 10, line 4, Posanski describes the compositions as not being aqueous, meeting the requirement to exclude a hydrophilic phase and that the amounts in the examples meet the amounts in the claims.

In response to the rejection, Applicant has amended independent Claims 11 and 17 by indicating that the therapeutic agent is selected from the group consisting of rapamycin, tacrolimus, and mycophenolate-mofetil, none of which are taught by Posanski. Since Posanski teaches pharmaceutical compositions containing only cyclosporin as an active ingredient, Posanski does not teach the specific therapeutic agents shown in presently amended Claims 11 and 17. Thus, the presently claimed invention is distinguished from Posanski. Applicant therefore respectfully requests withdrawal of the rejection of Claims 11-14 and 16-19 under 35 USC § 102(b).

In the final office action of November 26, 2008, Claims 19 and 20 remain rejected under 35 U.S.C. §103(a) as allegedly obvious over Posanski (GB 2 228 198 A).

Posanski has been cited for allegedly teaching an oral formulation (title, abstract). Although Posanski does not specifically teach tablets or capsules as recited in present Claim 20, the Examiner's position is that tablets and capsules are oral dosage forms. The Examiner

alleges that taking the broad teaching of Posanski, one having ordinary skill in the art would have a reasonable expectation of success in formulating the dosage form of Posanski in tablet or oral dosage form for oral administration.

Applicant respectfully traverses the rejection of Claims 19-20 as allegedly obvious for the following reasons. Applicant has amended Claim 11, from which Claims 19 and 20 depend, by indicating that the therapeutic agent is selected from the group consisting of rapamycin, tacrolimus, and mycophenolate-mofetil, none of which are taught or suggested by Posanski.

Applicant submits that the state of the art as of the filing date of the present application did not suggest to a skilled person to precisely combine the excipients according to Claim 11 to achieve a pharmaceutical composition comprising rapamycin, tacrolimus or mycophenolate-mofetil having good oral bioavailability. Furthermore, Posanski does not disclose the sorbitan fatty acid ester co-surfactant according to Claim 11, having an HLB of less than 10, as an essential requirement. Moreover, Posanski clearly teaches away from using an additional co-surfactant according to the present invention (See last paragraph on page 9 to page 10 of Posanski).

Applicant respectfully submits that there is no suggestion in Posanski that the presently claimed formulation as presently recited in Claim 11 could or should be made. Since there is no suggestion in Posanski that the composition recited in Claim 11 could or should be made, one skilled in the art at the time the invention was made, would not have found it obvious to practice the process of Claims 19 and 20. Applicant therefore respectfully request withdrawal of the rejection of Claims 19 and 20 under 35 USC § 103(a).

In the final office action of November 26, 2008, Claims 11-20 remain rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Cavanak (U.S. Pat. 5,639,724).

Cavanak has been cited for allegedly teaching a composition containing cyclosporin as the active ingredient, glycerol fatty acid ester and a tenside having an HLB of 10. The Examiner has alleged that Cavanak describes a variety of cyclosporin compositions that contain sesame oil, Tween or Cremophor, triglyceride, neutral oils and tri- and di-glycerides, Cremophor and sorbitan monolaurate and the process of combining the components into the formulation. The

Examiner has further asserted that Cavanak contemplates oral dosages of granules, tablets, capsules and drink solutions.

Applicant respectfully traverses the rejection of Claims 11-20 as allegedly obvious for the following reasons. Cavanak teaches a composition containing cyclosporine as the sole active agent, glycerol fatty acid ester and tenside having HLB of 10. Applicant has amended Claim 11, from which process Claims 19 and 20 depend, and Claim 17 by indicating that the therapeutic agent is selected from the group consisting of rapamycin, tacrolimus, and mycophenolate-mofetil, none of which are taught or suggested by Cavanak. Applicant respectfully submits the fact that individual excipients are known for pharmaceutical use does not make their combination obvious since the interaction between individual excipients and their effect on a drug's bioavailability, which is critical for the patient, and other properties, could not be accurately predicted by a skilled person.

The hydrophobic nature of active substances according to Claim 11 presents particular problems with regard to providing pharmaceutically acceptable oral formulations. In the case of drugs which are sparingly soluble in water, the amount which can be resorbed is diminished, resulting in reduced bioavailability, biological variability and undesirable variations in efficacy. Reduced variability is a very important property in immunosuppressive therapy, in view of the importance of maintaining drug concentration within a therapeutic window. Only particular combinations of excipients are capable of achieving good bioavailability, high stability and low variability within and between patients. The formulation according to the present invention is such a formulation. Good and stable bioavailability are very critical in the field of immunosuppression, such as transplantation, for a patient taking rapamycin, tacrolimus or mycophenolate-mofetil since an overdose would lead to severe side effects and an underdose to graft rejection and ultimately to graft loss.

Applicant submits that the state of the art at the filing date of the present invention did not suggest to a skilled person to precisely combine the excipients according to Claim 11 to achieve a pharmaceutical composition comprising rapamycin, tacrolimus or mycophenolate-mofetil having good oral bioavailability. Furthermore, Cavanak does not disclose the sorbitan fatty acid ester co-surfactant according to Claim 11, having an HLB of less than 10, as an essential element.

Applicant submits that Cavanak does not disclose or suggest that a combination of a co-surfactant with an HLB of less than 10, a suitable oil and a surfactant with an HLB of more than 10 would lead to formulations providing adequate oral bioavailability for rapamycin, tacrolimus or mycophenolate-mofetil. Even though the present invention may appear to be simple, Applicant respectfully submits that this is only with hindsight and an ex-post facto analysis.

Applicant respectfully submits that there is no suggestion or motivation in Cavanak that the presently claimed formulation as presently recited in amended Claims 11 and 17 could or should be made. Since there is no suggestion in Cavanak that the composition or process recited could or should be made or carried out, one skilled in the art at the time the invention was made would not have found it obvious to make the composition or practice the process claimed. Applicant therefore respectfully request withdrawal of the rejection of Claims 11-20 under 35 USC § 103(a).

Claims 11-20 have been rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over Claims 1, 27-35 and 37; Claims 1-10; and Claims 1-10 of copending Application Nos. 11/453,504, 10/961,785 and 10/623,887, respectively. The Examiner has alleged that Claims 11 and 13 of the present application read on at least Claims 1 and 3 of co-pending Application Nos. 10/961,785 and 10/623,887 and Claims 1, 27, 29, 31-33 and 37 of co-pending Application No. 11/453,504.

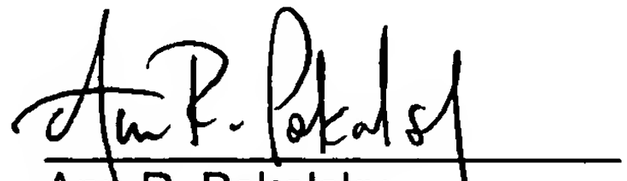
Applicant submits that Claim 13 has been canceled. Further, Applicant submits that since Claims 11 and 17 are presently amended by indicating that the therapeutic agent is selected from the group consisting of rapamycin, tacrolimus, and mycophenolate-mofetil, Claim 11 does not read upon any of the claims of copending Application Nos. 10/961,785 and 11/453,504 (which has issued as U.S. Patent No. 7,511,041 on March 31, 2009). The claims in the cited applications are directed towards compositions comprising cyclosporine as the therapeutic agent. Applicant therefore respectfully requests withdrawal of the rejection of Claims 11-20 on the ground of nonstatutory obviousness-type double patenting with respect to copending Application Nos. 10/961,785 and 11/453,504.

With respect to the provisional rejection of Claims 11-20 on the ground of nonstatutory obviousness-type double patenting over Claims 1-10 of copending Application No. 10/623,887,

Applicant will consider filing a terminal disclaimer upon allowance of the claims under consideration is this application.

In view of the foregoing remarks and amendments, it is respectfully submitted that the pending claims are in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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